Polygenic risk scores for bipolar disorders associated with worse global functioning

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BACKGROUND

Polygenic risk scores for bipolar disorders (PRS-BD) have been related to clinical variables and individual characteristics.[1-3] The aim of this preliminary study was to investigate the association between genetic risk for bipolar disorders (BD) with measures of global functioning.

METHODS

PRS-BD were calculated for adult participants (18-61 years old) with BD and healthy controls using PRSice-2 based on summary statistics from the Psychiatric Genomic Consortium. The psychiatric diagnosis was established according to the Diagnostic and Statistical Manual of Mental Disorders Fourth Edition - Text Revision (DSM-IV-TR). Generalized linear models with robust estimator analyzes were performed to investigate the association between PRS-BD z scores with functioning, measured by the Global Assessment of Functioning (GAF). Demographic and clinical variables that presented a significant association or a trend for association (p<0.20) with the outcome in the bivariate analyzes were included as a covariate in the model, in addition to ethnicity, to examine the independent association between PRS-BD and GAF.

RESULTS

203 participants (145 females [71.4%] and 58 males [28.6%]) were evaluated: 133 (65.5%) with BD type I diagnosis, 18 (8.9%) with BD type II and 52 (25.6%) healthy controls (Table 1). PRS-BD presented a weak and significant correlation with lower GAF (Spearman correlation r= -0.17, p=0.01) (Figure 1). Table 2 shows the generalized linear models analyzes between the independent variables and GAF (Table 2). The association between PRS-BD and GAF remained statistically significant when controlling for ethnicity, depressive and manic/hypomanic symptoms in the generalized linear models with covariates (B coefficient -3.99 [-6.62 – -1.37 95% CI] p=0.01) (Table 3). Figure 2 shows PRS-BD z scores distribution between the three groups.

CONCLUSION

Genetic risk for BD could confer a risk for worse global functioning regardless of psychiatric symptoms. Among the limitations, the lack of controlling for genetic background of the sample should be highlighted.

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Table 1. Socio-demographics, clinical and functioning characteristics of the sample

	Healthy controls (HC) 52 (25.6%)	BD II 18 (8.9%)	BD I 133 (65.5%)	Pearson chi²/test statistic[a] (p value)	Post-hoc p value
Demographics					
Female gender n (%)	35 (67.3)	17 (94.4)	93 (69.9)	5.25 (0.07)	-
Age median (IQR)	34 (26 – 42)	43.5 (27.7 – 53)	34 (29 – 44)	4.41 (0.11)	-
Ethnicity Hispanic or Latino[b] n (%)	11 (21.2)	4 (22.2)	29 (22)	0.02 (0.99)	-
Race Non-Hispanic white or Caucasian[c]	14 (26.9)	9 (50)	49 (37.1)	10.12 (0.61)	-
Clinical					
	median (IQR)	**median (IQR)**	**median (IQR)**		
PRS z scores	-0.34 (-1.07 – 0.57)	0.37 (-0.29 – 0.64)	0.18 (-0.58 – 0.82)	4.42 (0.11)	-
MADRS	0 (0 – 0)	17 (3 – 24)	11.5 (3.2 – 22.7)	86.30 (<0.001)	<0.001[d]
YMRS	0 (0 – 0)	3.5 (0 – 7)	4 (1 – 9)	63.34 (<0.001)	<0.001[d]
Total number of hospitalizations	-	1 (0 – 2)	3 (1 – 5)	14.42 ((<0.001)	-
Number of hospitalizations – depression	-	0.5 (0 – 2)	1 (0 – 2.7)	1.15 (0.28)	-
Number of hospitalizations – mania	-	0 (0 – 0)	1 (0 – 3)	18.32 (<0.001)	-
Age at first hospitalization	-	29 (24 – 46.2)	24 (18 – 30)	4.15 (0.04)	-
Global Assessment of Functioning	90 (87 – 92.7)	59 (52.7 – 70)	54.5 (45 – 65)	112.78 (<0.001)	<0.001[d]

[a]Kruskal-Wallis test with Dunn's post-hoc; [b]vs. non-Hispanic or Latino; [c]Other races include Hispanic or Latino, Black or African American, American Indian or Alaskan, Asian, Hawaiian or Pacific Islander or responded as more than one race; [d]HC vs. BD I and HC vs. BD II; BD I/II: Bipolar Disorders type I or II; IQR: interquartile range: MADRS: Montgomery-Asberg Depression Scale; PRS: polygenic risk scores; YMRS: Young Mania Rating Scale.

Table 2. Generalized linear models* analyzes between the independent variables and global functioning[a]

	B coefficient	95% CI	p value
Demographics			
Gender	-1.47	-7.36 – 4.42	0.62
Age	0.03	-0.21 – 0.27	0.80
Ethnicity	4.01	-2.61 – 10.62	0.23
Race	0.21	-1.32 – 1.74	0.79
Clinical			
PRS z scores	-3.99	-6.62 – -1.37	0.003
MADRS	-1.20	-1.37 – -1.02	<0.001
YMRS	-1.49	-1.77 – -1.02	<0.001

*robust estimator; [a]Measured by the Global Assessment of Functioning (GAF); CI: confidence interval.

Table 3. Generalized linear models* showing the independent association with global functioning[a]

Variables	B coefficient	95% CI	p value
Ethnicity	-2.09	-6.19 – 2.01	0.32
PRS z scores	-2.28	-3.95 – -0.61	0.01
MADRS	-0.99	-1.15 – -0.83	<0.001
YMRS	-1.05	-1.28 – -0.83	<0.001

*robust estimator; [a]Measure by the Global Assessment of Functioning.

Figure 1. Scatterplot with Polygenic Risk Scores and Global Assessment of Functioning

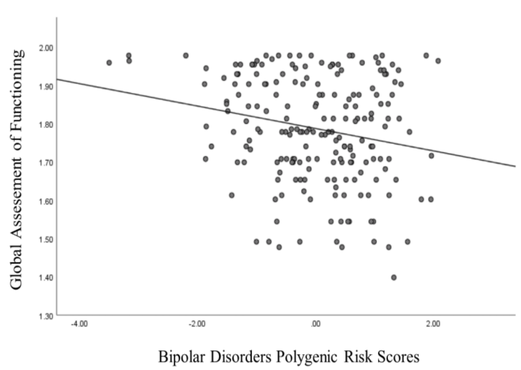
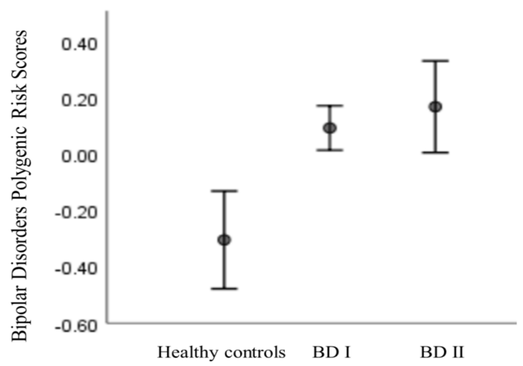


Figure 2. Distribution of the Polygenic Risk Scores (z scores) between the three groups (simple error bar ± SEM)



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